ROSIGLITASONE EFFECT ON THE INSULIN SIGNALING IN GRANULOSA CELLS OF PATIENTS WITH PCOS
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Metabolic abnormalities such as hyperinsulinemia, insulin resistance and obesity are features of Polycystic Ovarian Syndrome (PCOS), with a significant role in its pathogenesis. PPARγ and FoxO1 are key transcription factors that regulate the metabolism of glucose, insulin response and are linked with insulin resistance. Insulinsensitizer drugs as thiazolidinediones improve metabolic syndrome in PCOS patient. Objectives: Determine the effect of PPARγ agonist (Rosiglitazone Rz) on: 1) Activation of Insulin signaling pathway, insulin receptor-IRS1-Akt 2) Expression of FoxO1/ pFOXO1 3) Glucose transport and GLUT4 transporter expression in luteinized granulosa cells GC of normal and PCOS women. Methodology: The GC were obtained from PCOS patients n = 15 and patients with male factor infertility control = 20 of the IDIMI IVF program. IRS1 / p-IRS1, Akt/pAkt, PPARγ, FoxO1/pFoxo1 and GLUT4 were assessed by Western blot. Glucose transport was determined by incorporation of tritiated glucose in basal conditions and after stimulation with Rz. Results: PCOSGC have higher levels of pIRS1 in serine residues, inactivating phosphorylation of insulin signaling, low levels of total Akt and phosphorylated compared with control p<0.05. PCOSGC show higher levels of FOXO1 and lower levels of pFOXO1. In vitro treatment with 0.1 ?M Rz decreases IRS1serine phosphorylation and improve pAKT levels in PCOSGC. Rz decreases FOXO1 levels and improved pFOXO1 after stimulation with insulin in PCOSGC. Rz increases glucose uptake and increases GLUT4 levels basally decreased in PCOSGC. Conclusions: RZ not only increases expression of GLUT4, it also modulates the insulin signaling pathway in granulosa cells of PCOS improving insulin resistance of these cells. PPARγ agonists administration us RZ can take important therapeutic rol, improving transport of glucose into ovarian cells, contributing to a better oocyte quality and maturation.